

11 December 2017

Radium-223-dichloride (▼ Xofigo): Increased risk of death and fractures in a randomised clinical trial with Xofigo used in combination with abiraterone acetate and prednisolone/prednisone

Dear Healthcare Professional,

Bayer AG in agreement with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA) would like to inform you of the following:

Summary

An increased incidence of deaths and fractures has been identified in a randomised clinical trial in patients with chemotherapy-naïve metastatic castration-resistant prostate cancer (CRPC) receiving radium-223 dichloride in combination with abiraterone acetate and prednisone/prednisolone (15396/ERA-223 study).

Until the full analysis of the results is completed, the following is recommended:

- **Do not use radium-223 dichloride in combination with abiraterone acetate and prednisone/prednisolone in patients with metastatic castration-resistant prostate cancer.**

Background on the safety concern

Xofigo is approved for the treatment of men with castration-resistant prostate cancer, symptomatic bone metastases and no known visceral metastatic disease.

Preliminary data from a randomised, double blind, placebo controlled study, showed that there was an increased incidence of fractures (24% vs 7%) and deaths (27% vs 20%) among patients receiving Xofigo in combination with abiraterone acetate and prednisone/prednisolone (n=401) compared to patients receiving placebo in combination with abiraterone acetate and prednisone/prednisolone (n=405). This study in asymptomatic or mildly symptomatic chemotherapy-naïve patients with bone predominant metastatic CRPC was unblinded early based on an Independent Data Monitoring Committee recommendation.

The measures outlined above should be followed while there is further investigation of the implications of these findings. Further advice will be communicated as appropriate at the end of the review.

Call for reporting

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme. It is easiest and quickest to report ADRs online via the Yellow Cards website - <https://yellowcard.mhra.gov.uk/>

Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gsi.gov.uk
- at the back of the British National Formulary (BNF)
- by telephoning the Yellow Card Information Service free phone line: 0800-731-6789
- or by downloading and printing a form from the Yellow Card section of the MHRA website

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, product brand name and batch number

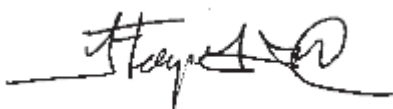
You can also report suspected adverse drug reactions to Bayer via email: pvuk@bayer.com

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 of the SmPC for how to report adverse reactions.

Company contact point

Contact point details for further information are given in the product information of the medicinal products (SmPC and PL) at: <http://www.ema.europa.eu/ema/> or contact Bayer plc Medical Information directly (telephone: 0118 206 3116, e-mail: medical.information@bayer.co.uk).

Yours faithfully,

A handwritten signature in black ink, appearing to read 'Luis-Felipe Graterol', written over a horizontal line.

Dr Luis-Felipe Graterol
Medical Director
Bayer plc